Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1-20 (Cancelled).

21. (Currently amended) A method of treating a bone disease in a patient in need thereof, comprising orally administering to the patient a pharmaceutical formulation comprising

(a) a core containing a bone disease treating effective amount of ibandronate and

(b) a coating which is free of ibandronate,

wherein the coating dissolves or is separated from the core during contact with digestive solution in the patient's stomach, and wherein said coating comprises at least one member selected from the group consisting of a cationic copolymer of dimethylaminoethyl methacrylate with neutral methacrylic esters, a copolymer selected from the group consisting of ammonio methacrylate copolymer Type A or Type B USP/NF, Eudragit® RL and Eudragit® RS ~~of acrylic and methacrylic esters which has a low content of quaternary ammonium groups~~, a copolymer of ethyl acrylate and methyl methacrylate with neutral character, an anionic copolymer of methacrylic acid and methyl methacrylate, cellulose acetate phthalate, cellulose acetate trimellitate, methylhydroxypropylcellulose phthalate and polyvinyl acetate phthalate,

wherein the pharmaceutical formulation avoids release of ibandronate in the esophagus, and

wherein at least 30% of the administered amount of ibandronate is released from the pharmaceutical formulation into the stomach.

22. (Previously presented) The method of claim 21, wherein the bone disease is related to a disorder in calcium metabolism.

23. (Previously presented) The method of claim 21, wherein the bone disease is selected from the group consisting of hypercalcemia, osteoporosis, tumor osteolysis and Paget's disease.

24. (Previously presented) The method of claim 21, wherein at least 75% of the administered amount of ibandronate is released from the pharmaceutical formulation into the stomach.

25. (Previously presented) The method of claim 21, wherein at least 85% of the administered amount of ibandronate is released from the pharmaceutical formulation into the stomach.

26. (Previously presented) The method of claim 21, wherein at least 30% of the administered amount of ibandronate is released from the pharmaceutical

formulation into the stomach in less than 2 hours after the pharmaceutical formulation contacts the digestive solution in the patient's stomach.

27. (Previously presented) The method of claim 21, wherein at least 75% of the administered amount of ibandronate is released from the pharmaceutical formulation into the stomach in less than 2 hours after the pharmaceutical formulation contacts the digestive solution in the patient's stomach.

28. (Previously presented) The method of claim 21, wherein at least 85% of the administered amount of ibandronate is released from the pharmaceutical formulation into the stomach in less than 2 hours after the pharmaceutical formulation contacts the digestive solution in the patient's stomach.

29. (Previously presented) The method of claim 21, wherein at least 30% of the administered amount of ibandronate is released from the pharmaceutical formulation into the stomach in less than 1 hour after the pharmaceutical formulation contacts the digestive solution in the patient's stomach.

30. (Previously presented) The method of claim 21, wherein at least 75% of the administered amount of ibandronate is released from the pharmaceutical formulation into the stomach in less than 1 hour after the pharmaceutical formulation contacts the digestive solution in the patient's stomach.

31. (Previously presented) The method of claim 21, wherein at least 85% of the administered amount of ibandronate is released from the pharmaceutical formulation into the stomach in less than 1 hour after the pharmaceutical formulation contacts the digestive solution in the patient's stomach.

32. (Previously presented) The method of claim 21, wherein at least 30% of the administered amount of ibandronate is released from the pharmaceutical formulation into the stomach 1-30 minutes after the pharmaceutical formulation contacts the digestive solution in the patient's stomach.

33. (Previously presented) The method of claim 21, wherein at least 75% of the administered amount of ibandronate is released from the pharmaceutical formulation into the stomach 1-30 minutes after the pharmaceutical formulation contacts the digestive solution in the patient's stomach.

34. (Previously presented) The method of Claim 21, wherein at least 85% of the administered amount of ibandronate is released from the pharmaceutical formulation into the stomach 1-30 minutes after the pharmaceutical formulation contacts the digestive solution in the patient's stomach.

35. (Previously presented) The method of claim 21, wherein about 80-90% of the administered amount of ibandronate is released from the pharmaceutical

formulation into the stomach within 15 minutes after the pharmaceutical formulation contacts the digestive solution in the patient's stomach.

36. (Canceled)

37. (Previously presented) The method of claim 21, wherein the coating further comprises at least one cellulose derivative selected from the group consisting of methylcellulose, hydroxymethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, methylhydroxyethylcellulose, methylhydroxypropylcellulose, sodium carboxymethylcellulose and ethylcellulose.

38. (Currently amended) The method of claim 21, wherein the coating comprises at least one member selected from the group consisting of a cationic copolymer of dimethylaminoethyl methacrylate with neutral methacrylic esters, a copolymer selected from the group consisting of ammonio methacrylate copolymer Type A or Type B USP/NF, Eudragit® RL and Eudragit® RS ~~of acrylic and methacrylic esters which has a low content of quaternary ammonium groups~~ and a copolymer of ethyl acrylate and methyl methacrylate with neutral character.

39. (Previously presented) The method of claim 21, wherein the coating comprises at least one member selected from the group consisting of an anionic copolymer of methacrylic acid and methyl methacrylate, cellulose acetate

phthalate, cellulose acetate trimellitate, methylhydroxypropylcellulose phthalate and polyvinyl acetate phthalate.

40. (Currently amended) In a method of treating bone disease in a patient in need thereof, wherein said method comprises orally administering to a patient a pharmaceutical formulation containing ibandronate, the improvement comprising (a) a core containing a bone disease treating effective amount of ibandronate and (b) a coating which is free of ibandronate surrounding the core, wherein the coating dissolves or is separated from the core during contact with digestive solution in the patient's stomach, wherein said coating comprises at least one member selected from the group consisting of a cationic copolymer of dimethylaminoethyl methacrylate with neutral methacrylic esters, a copolymer selected from the group consisting of ammonio methacrylate copolymer Type A or Type B USP/NF, Eudragit® RL and Eudragit® RS ~~of acrylic and methacrylic esters which has a low content of quaternary ammonium groups~~, a copolymer of ethyl acrylate and methyl methacrylate with neutral character, an anionic copolymer of methacrylic acid and methyl methacrylate, cellulose acetate phthalate, cellulose acetate trimellitate, methylhydroxypropylcellulose phthalate and polyvinyl acetate phthalate, and wherein the coating prevents irritation and ulcerations of the esophagus, and wherein at least 30% of the administered amount of ibandronate is released from the pharmaceutical formulation into the stomach.

41. (Currently amended) A method of treating a bone disease in a patient in need thereof, comprising orally administering to the patient a pharmaceutical formulation comprising (a) a core containing a bone disease treating effective amount of ibandronate and (b) a coating which is free of ibandronate, wherein the thickness and type of the coating is chosen so that when the pharmaceutical formulation is administered orally to the patient, release of the ibandronate in the esophagus is avoided, the coating dissolves or is separated from the core during contact with digestive solution in the patient's stomach, and at least 30% of the administered amount of ibandronate is released from the pharmaceutical formulation into the stomach and wherein said coating comprises at least one member selected from the group consisting of a cationic copolymer of dimethylaminoethyl methacrylate with neutral methacrylic esters, a copolymer selected from the group consisting of ammonio methacrylate copolymer Type A or Type B USP/NF, Eudragit® RL and Eudragit® RS ~~of acrylic and methacrylic esters which has a low content of quaternary ammonium groups~~, a copolymer of ethyl acrylate and methyl methacrylate with neutral character, an anionic copolymer of methacrylic acid and methyl methacrylate, cellulose acetate phthalate, cellulose acetate trimellitate, methylhydroxypropylcellulose phthalate and polyvinyl acetate phthalate.

Remarks:

In the Office Action dated August 11, 2006, claims 21-41, in the above-identified U.S. patent application were rejected. Reconsideration of the rejections is respectfully requested in view of the above amendments and the following remarks. Claims 21-35 and 37-41 remain in this application and claims 1-20 and 36 have been canceled.

Claims 21-41 were rejected under 35 USC §112, second paragraph as indefinite. Though applicants respectfully disagree, the claims have been amended to recite "a copolymer selected from the group consisting of ammonio methacrylate copolymer Type A or Type B USP/NF, Eudragit® RL and Eudragit® RS". This amendment is supported by the disclosure on page 6, lines 25-29, of the present application. In view of these amendments applicants request that this rejection be withdrawn.

Claims 21-41 were rejected under 35 USC §103(a) as unpatentable over CA 2,149,052 in view of EP 0 421 921 A1 and Canadian Pat. 1,305,166. Applicants respectfully point out that the prior art does not suggest or disclose a coating that dissolves or is separated from the core during contact with digestive solution in the patient's stomach. Though EP 0421 921 may disclose similar ingredients as the coating in the present invention, the present claims are method claims which require the coating to dissolve or separate from the core during contact with the digestive solution in the patient's stomach. EP 0421 921 discloses enterically coated granulates specifically formulated for rapid transition to the intestine in order to avoid adverse effects. EP 0421 921 releases the drug

in the intestine not in the stomach due to the outer gastric juice resistant coating containing an acrylic acid-methacrylic acid copolymer. CA 2,149,052 discloses a method for preparing tablets containing bisphosphonates by direct compression. The tablet may be coated but there is no suggestion or disclosure that the coating should dissolve or separate from the core during contact with digestive solution in the patient's stomach and thus combining Canadian Pat. 2,149,052 with EP 0421 921 would lead to a formulation which does not dissolve in the patient's stomach. Canadian Pat. 1,305,166 does not cure this deficiency because Canadian Pat. 1,305,166 does not indicate that the coating should dissolve or separate from the core either. Even though the present claims encompass additional substances in the coating as stated in the office action, the claims require the coating to dissolve or separate from the core during contact with the digestive solution in the patient's stomach. In other words, other components which prevent the coating from dissolving or separating from the core during contact with the digestive solution in the patient's stomach are not part of the present invention. Since none of the cited references disclose treating a bone disease with a formulation which has a core containing ibandronate and a coating which dissolves or separates from the core in the patient's stomach, applicants contend that the presently claimed invention would not be obvious in view of the prior art and request that this rejection be withdrawn.

Applicants respectfully submit that all of claims 21-35 and 37-41 are now in condition for allowance. If it is believed that the application is not in condition

for allowance, it is respectfully requested that the undersigned attorney be contacted at the telephone number below.

In the event this paper is not considered to be timely filed, the Applicant respectfully petitions for an appropriate extension of time. Any fee for such an extension together with any additional fees that may be due with respect to this paper, may be charged to Counsel's Deposit Account No. 02-2135.

Respectfully submitted,

By 

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